



The Effectiveness of Enteral Nutrition Support in the Growth of Children Patients with Cancer

Kanserli Çocuk Hastaların Büyümesinde Enteral Beslenme Desteğinin Etkinliği

The Enteral Nutrition Support in Children with Cancer

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Özet

Amaç: Bu çalışmanın amacı, kemoterapi alan kanserli çocuklarda antropometrik ve biyokimyasal parametreler aracılığıyla, enteral beslenme desteğinin büyümede olumlu etkisini araştırmaktır. **Gereç ve Yöntem:** Yeni tanı almış ve yoğun kemoterapi alan ardışık 43 pediatrik kanserli hasta çalışmaya dahil edildi. Yirmi altı hasta enteral beslenme formülüsü aldı. Onyeddi kontrol hastası enteral beslenme formülüsü almadı. Antropometrik parametreleri (boy, kilo, vücut kitle indeksi, triseps, subskapular ve suprailiac deri kıvrım kalınlığı), serum albümin, prealbumin, transferrin düzeyleri ve lipid profilleri tanı anında ve 3. ayda ölçüldü. **Bulgular:** 3 ayın sonunda enteral beslenme alan grupta subskapular ve suprailiac deri kıvrım kalınlıklarında tanı anındaki ölçülerle karşılaştırıldığımızda belirgin bir artış saptadık ($p=0.01$ ve $p=0.014$ sırasıyla). Prealbumin ve albümin değerlerinde enteral beslenme desteğinin 3. ayında artış saptandı ($p=0.005$ ve $p=0.006$, sırasıyla). Enteral beslenme alan grubunun % 69.2'inde tedavi sonunda ağırlık persentil artışı görüldü. Üçüncü ayda, albümin ve suprailiac deri kıvrım kalınlıkları değerleri enteral beslenme grubunda, kontrol grubuna göre yüksek idi ($p=0.012$ ve $p=0.017$, sırasıyla). Üçüncü ayda kontrol grubunun antropometrik ve biyokimyasal parametrelerinde tanı anı ile karşılaştırıldığında anlamlı bir değişiklik görülmedi. **Tartışma:** Bu çalışma enteral beslenme formülüsü alan kanserli çocuklarda antropometrik ve biyokimyasal parametrelerde iyileşme göstermektedir.

Anahtar Kelimeler

Antropometrik Parametre; Biyokimyasal Parametre; Enteral Beslenme; Çocuk; Kanser

Abstract

Aim: The purpose of this study was to assess, through anthropometric and biochemical parameters, the positive effect on growth of enteral nutrition support in children with cancer receiving chemotherapy. **Material and Method:** Forty-three consecutive patients newly diagnosed with pediatric malignant disease and receiving intensive chemotherapy were included. Twenty-six patients received an enteral nutrition formula. Seventeen control patients did not receive enteral nutrition formula. Anthropometric parameters (weight, height, body mass index, triceps, subscapular and suprailiac skinfold thickness), serum albumin, prealbumin and transferrin levels and lipid profiles were measured at time of diagnosis and the 3rd month. **Results:** At the end of 3 months we determined a marked increase in subscapular and suprailiac skin fold thicknesses in the enteral nutrition group compared to at time of diagnosis ($p=0.01$ and $p=0.014$, respectively). Prealbumin and albumin values increased considerably after 3 months of enteral nutrition formula support ($p=0.005$ and $p=0.006$, respectively). Weight percentile increment was determined (69.2% of patients) in the enteral nutrition group compared to at time of diagnosis. At 3 months, albumin and suprailiac skinfold thicknesses values were higher in the enteral nutrition group as compared to controls ($p=0.012$ and $p=0.017$, respectively). There were no significant changes in anthropometric and biochemical parameters in the control group at the end of treatment compared to at time of diagnosis. **Discussion:** This study demonstrates an improvement in anthropometric and biochemical parameters in children with cancer receiving an enteral nutrition formula.

Keywords

Anthropometric Parameter; Biochemical Parameter; Enteral Nutrition; Children; Cancer

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Introduction

Malnutrition in pediatric patients with malignancies is a major medical problem [1]. The malnutrition levels are as high as 17% in children with newly diagnosed localized tumors and 37% in subjects with metastatic disease. Modern pediatric cancer treatment affects normal as well as malignant tissues and is thus capable of causing specific nutritional problems [2].

Nutrition assessment represents the first step in clinical nutrition management in pediatric oncology patients [3]. This assessment includes medical history, physical examination, biochemical and hematological data, such as visceral proteins, blood glucose levels, and lipid profiles, hemoglobin, hematocrit and lymphocyte counts, anthropometric measurements, and food and nutrition history. Visceral proteins such as prealbumin, transferrin and retinol-binding protein have emerged as indicators of nutritional status [4,5]. Anthropometric measurements are a primary component of the nutrition assessment process in pediatric oncology patients. The most sensitive indices for growth in children include weight, height for age and body mass index (BMI) [5]. Anthropometric measurements, including middle upper arm circumference, triceps, biceps, suprailliac and subscapular skinfolds and arm muscle mass, are preferred indicators of body composition in oncology patients [1,3]. Midarm circumference and triceps and biceps skinfolds have been reported to be more accurate indicators of malnutrition at diagnosis than weight and height indices [3].

Early indication for enteral nutrition therapy is one of the main goals of nutritional therapy in children and adolescents with cancer. Given the importance of individualized nutritional support to pediatric cancer patients, this should be an integral component of their overall treatment. The patients receiving enteral nutrition therapy in this study either maintained or achieved significant improvements in nutritional status, thus demonstrating the importance of nutritional support and follow-up during hospitalization [6]. Enteral nutrition is less expensive and more physiological than parenteral nutrition and also minimizes the risk of bacterial translocation by maintaining the integrity of the intestinal mucosa [3]. Enteral nutrition therapy requires a multidisciplinary team if children and adolescents with cancer are to be adequately supported [6].

Adequate nutrition assessment and management can reduce mortality and complications, optimize cancer care and minimize the deleterious effects of malnutrition that may be a consequence of the cancer itself or of the treatment administered. The aim of this study was to determine the importance of enteral nutrition support and to review nutritional assessment in children being treated in a pediatric oncology and hematology department.

Material and Method

This was a prospective, randomized, single-center study of sixty-one patients were newly diagnosed with cancer, aged 1–16 years, between October 2009 and October 2010. Forty-four of these patients were administered enteral nutrition formulae. Patients who were diagnosed with pediatric malignant disease and receiving intensive chemotherapy were consecutively selected to participate in the study. Twenty-six patients received enteral nutrition formulae (Resource Support™, Isosour Ju-

nior™) regularly during the study period. Eighteen patients used other enteral nutrition formulae available on the market. The 17 patients in the control group did not use any enteral nutrition formulae (due to the taste, nausea, vomiting, mucositis and loss of appetite). Fourteen patients who received Resource Support™, 12 patients who received Isosource Junior™ and 17 control groups were included into our study. The study protocol was approved by the Institutional Ethics Committee. Written consent was obtained from family or legal guardians and children over 12 years, and verbal assent for children under 12 years. Demographic data including name, gender, date of birth, date of diagnosis and type of cancer were recorded. Chemotherapy and enteral nutrition formula were administered for 3 months. Anthropometric parameters (weight, height, body mass index, triceps, subscapular and suprailliac skinfold thickness), serum albumin, prealbumin, transferrin levels and lipid profiles were measured at time of diagnosis and at the 3rd month.

Anthropometric measurements: Weight, height and body mass index (BMI) were measured using standard techniques [7]. All measurements were obtained by the same researcher (C.A.). Weight (kg) was measured using electronic scales with a margin of error of 0.1 kg. Height (cm) was measured using stadiometer, with a margin of error of 0.1 cm. Body mass index was calculated by dividing weight in kilograms by the square of height expressed in meters (kg/m^2).

Skinfold thickness measurements: Skinfold thicknesses were measured in triplicate on the left side of the body using Harpenden skinfold calipers (triceps; halfway between the acromion process and the olecranon process, subscapular; approximately 20 mm below the tip of the scapula, at an angle of 45° to the lateral side of the body and suprailliac; approximately 20 mm above the iliac crest, in the axillary line). A single observer (C.A.) took all the measurements. All measurements were taken triplicate and averaged, the results being expressed in millimeters (mm) [8].

Biochemical tests: Venous samples were collected, and serum was analyzed for biochemical parameters on the same day. These parameters included concentrations of serum protein, albumin, prealbumin and transferrin and lipid profiles. These were analyzed on a Cobas 6000 Autoanalyzer (Roche Diagnostic GmbH, Mannheim, Germany) using commercial kits from Roche Diagnostic Products. Serum protein and albumin levels were measured using the quantitative colorimetry method. Prealbumin and transferrin levels were determined using immunoturbidimetric assay. Serum prealbumin values were considered normal between 20 and 40 mg/dl and serum transferrin values between 200 and 360 mg/dl. Patients' plasma lipid profiles were determined using standard enzymatic methods.

Enteral nutrition support: Resource Support™ (Laboratories provided by Nestlé Healthcare Nutrition, Turkey) and Isosour Junior™ (Laboratories provided by Nestlé Healthcare Nutrition, Turkey) products were administered for 3 months. Fourteen patients (53.8%) older than 4 years received Resource Support™ and 12 patients (46.2%) aged 1–4 years Isosource Junior™. Each 200 ml container of Resource Support™ contained 310 kcal and 18 g (23%) protein, 35.8 g (46%) carbohydrate, 10.6 g (31%) fat and 1 g eicosapentaenoic acid (EPA). Each 250 ml container of Isosource Junior™ contained 305 kcal and 6.75 g

(9%) protein, 42.5 g (56%) carbohydrate and 11.75 g (35%) fat. Two flavors, chocolate and vanilla, were employed in this study. A nurse specializing in nutrition was responsible for checking that the supplement was taken regularly. Patients were instructed to consume two containers of supplement per day (morning and evening).

Anthropometric measurements and biochemistry tests were performed at diagnosis and 3 months after initiation of treatment in the control and enteral nutrition groups. The two groups were compared in terms of anthropometric and biochemical parameters at diagnosis and 3 months after treatment.

Statistical analysis: Data are expressed as arithmetic mean \pm standard deviation (SD) for quantitative data and as percentages (%) for qualitative data. Values are presented as mean (minimum-maximum). Statistical comparisons among groups were performed using the Two-Independent Samples Test (Mann-Whitney U Test). All the collected data were analyzed on SPSS software, version 15. $p < 0.05$ was defined as statistically significant.

Results

Forty-three patients (12.0- 192.0 months of age) were randomized into the study. In the enteral nutrition group, 5 patients were diagnosed with leukemia and 21 had a solid tumor. In the control group, 3 patients were diagnosed with leukemia and 14 had a solid tumor. The enteral nutrition group consisted of 26 patients, 53.8% (n=14) male and 46.2% (n=12) female, with mean age at diagnosis of 74.7 months (range 12.0-192.0 months). Fourteen patients (53.8%) received Resource Support™ and 12 patients (46.2%) Isosource Junior™. The control group consisted of 17 patients, 52.9% (n=9) male and 47.1% (n=8) female, with a mean age at diagnosis of 81.4 months (range 12.0-180.0 months). Patients' demographic characteristics are presented in Table 1. Age, sex and underlying malignancy in the enteral nutrition groups were similar to those in the control group.

At time of diagnosis, we determined no statistically significant differences in terms of anthropometric and biochemical parameters (except for prealbumin) between the enteral nutrition and control groups. At time of diagnosis, prealbumin levels were significantly lower in the enteral nutrition group compared to the control group ($p=0.029$); however, at 3 months, there were no significant group differences in prealbumin levels ($P>0.05$). At the end of 3 months, albumin levels and suprailiac skinfold thicknesses in the enteral nutrition groups were significantly greater compared to control patients not given the enteral nutrition supplement ($p=0.012$ and $p=0.017$, respectively). The anthropometric and biochemical parameters exhibited no significant differences between time of diagnosis and at the end of 3 months in the control group.

At 3 months, in the enteral nutrition group, subscapular and suprailiac skinfold thicknesses improved compared to status at diagnosis of malignant diseases ($p=0.01$ and $p=0.014$, respectively) (Figure 1). Changes in values for weight, height, BMI and triceps skinfold thicknesses were not significant ($p<0.05$). At the end of treatment, patients exhibited a weight percentile increment (69.2% of patients). Although height increased at the end of treatment, there was no percentile change. The enteral nutrition group tended to have higher albumin and prealbumin levels

Table 1. Patients' demographic characteristics.

Groups (number of patients)	EN group (n=26)	Control group (n=17)
Age (mean /range) (months)	74.67 \pm 56.51 (12-192)	81.35 \pm 56.06 (12-180)
Sex (male/female)	14/12 (54/46%)	9/8 (53/47%)
Underlying malignancy		
Solid tumor	21 (81%)	14 (82%)
Acute leukemia	5 (19%)	3 (18%)

EN; Enteral nutrition

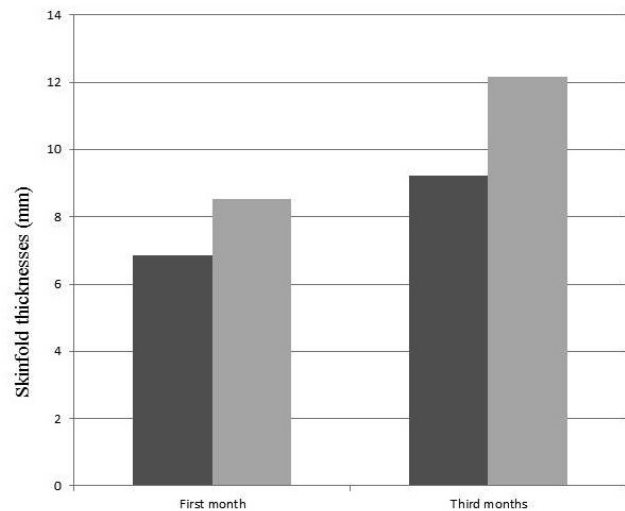


Figure 1. Enteral nutrition group patients' subscapular and suprailiac skinfold thicknesses at diagnosis and 3 months after treatment. Dark column: Subscapular skinfold thicknesses. Light column: Suprailiac skinfold thicknesses

after 3 months of treatment compared to at time of diagnosis ($p=0.005$ and $p=0.006$, respectively); however, serum protein, transferrin and lipid profiles were similar ($p>0.05$). Mean values of the anthropometric and biochemical parameters of all 43 patients are presented in Table 2.

Discussion

One of the main contributing cause of increased morbidity and mortality in cancer patients is malnutrition. Many studies have demonstrated that patients with cancer are malnourished. At time of diagnosis, approximately 75% of all cancer patients are found to be malnourished, and between 20% and 40% of these die due to malnutrition and related complications [9-12]. Assessment of nutritional status is difficult, however, because there is no "gold standard." Nutritional status in cancer patients is determined on the basis of anthropometry indexed to biochemical measurements in serum [1]. Several studies have recommended the use of arm anthropometry, including tricipital skinfold thickness and middle upper arm circumference, as appropriate indicators of body composition in pediatric oncology patients [1,13].

Chinceşan et al. [1] described tricipital skinfold thickness and middle upper arm circumference as accurate indicators of nutritional status in pediatric subjects with malignancy. Smith et al. [13] observed a malnutrition prevalence of 5% at time of diagnosis among children and adolescents with cancer based on z-scores of weight-for-height and height-for-age. However, in that same study, 20% and 23% of the patients were depleted on the basis of tricipital skinfold thickness and middle upper arm

Table 2. Patients' anthropometric and biochemical parameters.

Parameter	EN group Time of diagnosis (n=26) Mean±SD	EN group End of treatment (3 months) (n=26) Mean±SD	Control group Time of diagnosis (n=17) Mean±SD	Control group End of treatment (3 months) (n=17) Mean±SD
Anthropometric				
Weight (kg)	21.36±14.82	23.58±16.07	26.66±18.01	27.92±18.07
Height (cm)	111.11±30.73	113.00±30.25	117.65±32.26	119.50±32.34
BMI (kg/m ²)	15.56±2.55	16.58±2.89	17.14±4.26	17.31±4.10
Triceps ST (mm)	8.73±2.92	9.80±2.30	9.15±4.99	9.77±5.49
Subscapular ST (mm)	6.85±3.15	8.53±2.92 ^c	7.92±4.26	8.64±5.31
Suprailiac ST (mm)	9.21±4.08	12.17±5.09 ^{b,c}	9.93±6.90	9.46±7.16
Biochemical				
Protein (g/dl)	6.89±0.79	6.75±0.60	6.75±0.53	6.48±0.38
Albumin (g/dl)	3.90±0.59	4.37±0.48 ^{b,c}	3.84±0.42	3.99±0.25
Prealbumin (mg/dl)	14.38±9.21 ^a	17.55±5.01 ^c	16.78±5.51	17.12±5.78
Transferrin (mg/dl)	264.44±130.2	256.00±64.06	230.36±44.86	217.81±47.54
Lipid profile				
Total cholesterol (mg/dl)	157.27±50.96	144.31±29.39	169.00±49.98	151.76±35.37
HDL- cholesterol (mg/dl)	36.77±17.37	40.31±10.22	38.91±16.32	53.43±70.60
LDL- cholesterol (mg/dl)	92.46±29.36	81.73±27.04	99.12±43.42	93.71±34.21
Serum triglyceride (mg/dl)	142.96±98.71	116.23±49.24	117.065±58.23	115.53±45.44

^aStatistically significant at $p < 0.05$ as compared to time of diagnosis of control group.

^bStatistically significant at $p < 0.05$ as compared to end of treatment of control group

^cStatistically significant at $p < 0.05$ as compared to time of diagnosis of EN group

ST; Skinfold thicknesses, EN; Enteral nutrition.

circumference, respectively. These results demonstrate that anthropometry of the arm is more effective in detecting early malnutrition [13]. In our study, we observed a marked increase in subscapular and suprailliac skinfold thicknesses at the end of the study compared to at time of diagnosis in the enteral nutrition group. In addition, albumin levels and suprailliac skinfold thickness at the end of the 3rd month were markedly higher in the enteral nutrition group compared to the control group.

Jain et al. [14] evaluated anthropometric, hematological and biochemical parameters before initiating therapy and response to therapy, during monitoring of nutritional status of 44 children with newly diagnosed malignancy. They reported a malnutrition level of 56.8% by weight for age criteria; 25% had low total proteins, 20.5% low serum albumin and 27.3% low serum transferrin levels [14]. Kibirige et al. [10] reported that median weight:height ratio and serum albumin concentrations may be useful measurements in children newly diagnosed with leukemia to indicate which patients will require supplementary nutrition. Yu et al. [15] also reported that low plasma protein concentrations can be ascribed to mild malnutrition in children with newly diagnosed or relapsed leukemia. Merritt et al. [16] reported similar results in pediatric cancer patients, suggesting that abnormal serum albumin is a more common indicator of acute metabolic response to fever and infection than decreased body mass. The clinical usefulness of serum albumin, with a biological half-life of approximately 20 days, is restricted by its inability to identify short term nutritional status variations and by a tendency to extravascular extravasation. In contrast, the rapid turnover of prealbumin (with a much briefer half-life, of approximately 2 days), which is less influenced by changes in body fluids than serum albumin, allows cancer patients to be monitored on a day-to-day basis [17]. Elhasid et al. [17] evaluated biochemical indices rather than anthropometric indices among 50 children with solid tumors. They observed that 36% had lower prealbumin levels than normal at time of diagnosis. Based on those results they recommended prealbumin as the

most accurate test for assessing the nutritional status of children with solid tumors, both at time of diagnosis and throughout chemotherapy. Yariş et al. [18] reported a significant correlation between serum prealbumin and transferrin levels and the presence of malnutrition. Kurugöl et al. [19] evaluated nutritional status in 45 pediatric cancer patients. Children in the active disease group had lower prealbumin levels than those in the remission group. They concluded that only prealbumin is a reliable and sensitive indicator of mild and marginal malnutrition. They suggested that low prealbumin may be detected before malnutrition using anthropometric measurements. In our study, in the enteral nutrition group, mean levels of prealbumin and albumin were significantly lower at time of diagnosis of malignant diseases and prealbumin and albumin levels were significantly elevated at the end of treatment (3rd month). In contrast to Yariş et al. [18] mean transferrin levels were not elevated in our study.

Abnormal blood lipid profiles have also been associated with cancer. The lipid profile in cancer patients is characterized by low low-density lipoprotein-cholesterol, low high-density lipoprotein-cholesterol and relatively high serum triglycerides [20, 21]. Ghalaut et al. [22] showed that low lipid concentrations are associated with poor disease prognosis. They determined significantly increased total serum cholesterol, HDL-cholesterol and LDL-cholesterol concentrations after chemotherapy, but no significant increase in serum triglyceride and VLDL-C cholesterol concentrations. We did not identify a statistically significant correlation between serum total cholesterol, HDL-cholesterol LDL-cholesterol and serum triglyceride levels at diagnosis or end of treatment in the enteral nutrition group compared to the control group.

Nutritional support among children with cancer is now regarded as a significant addition to treatment [23]. Children may be at even greater risk for nutritional depletion than adults, since they have a faster metabolic rate, greater caloric needs for growth and development, and often receive more aggressive cancer treatment [24]. Dietary supplementation with EPA, a n-3 polyunsaturated fatty acid, may benefit cancer patients by modulating various features of the inflammatory response associated with metabolic changes, weight loss and muscle wasting. Bayram et al. [9] reported a decrease in cancer-induced weight loss in pediatric patients receiving a protein and energy-dense nutrition supplement containing EPA. In our study, weight loss decreased at the 3rd month of treatment in children receiving nutrition products containing EPA (Resource Support™), and marked increases were determined in subscapular skinfold thickness, suprailliac skinfold thickness and prealbumin and albumin values. Study limitations; our findings are limited due to the low number of patients and short follow-up period. Children with cancer undergoing chemotherapy were unable to consume any food products, including enteral nutrition formulae, due to the taste of the products and nausea, vomiting, mucositis and loss of appetite. Significant improvements in nutritional status were achieved in those patients receiving enteral nutrition support

therapy. Further studies should now be considered on the basis of our results.

Conclusions; Assessment of nutritional status should be performed at time of diagnosis and during treatment. This is essential for planning nutritional intervention. We think that nutritional support to prevent loss of body mass, improve clinical outcomes and enhance overall quality of life represents an integral part of treating children with cancer.

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Competing interests

The authors declare that they have no competing interests.

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